

Application No. 09/933,680
Amendment Dated 8/9/2004
Reply to Office Action of 5/10/2004

REMARKS/ARGUMENTS

By this Amendment, claims 1, 35, and 48 are amended, claims 7-9, 13-33, 38-40, 44 and 45 are canceled. Claims 1-6, 10-12, and 34-37, 41-43, and 46-49 are pending.

Regarding claim 1, line 4, the word "wherein" was canceled by the Amendment dated 10/22/03.

Amendment of claim 1 is supported by the disclosure on page 9, lines 2-8, amendment of claim 35 is supported by the disclosure on page 8, lines 10-25.

The Applicants gratefully acknowledge the allowance of subject matter of claims 43 and 44 and allowance of claims 46 and 47. Claim 43 is dependent from claim 1, which as amended obviate Examiner's rejections as described below. Claim 44 is canceled because it duplicates claim 46.

Claims 38-40 are canceled because of the cited prior art disclosing heterofunctional azide reagent.

Claim 45 is canceled because it duplicates claim 48.

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

Claim Rejections – 35 USC § 102

U.S. Patent No. 4,931,546

Claims 1-3, 10, 11, 34-37, 41, 42, 48 and 49 stand rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 4,931,546. This rejection is respectfully traversed. Claim 1

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as amended obviates the rejection.

MPEP §2131 provides in relevant part:

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

To anticipate a claim, the reference must teach every element of the claim. MPEP §2131.

U.S. Patent No. 4,931,546 does not expressly or inherently describe each and every element of the claimed invention, a method of treating an implantable biological tissue, said method comprising stabilizing glycosaminoglycans on the tissue and cross-linking proteins on the tissue, wherein the glycosaminoglycans stabilizing comprises contacting the tissue with (a) a water-soluble carbodiimide composition having a pH of 6.9 to 7.9 or (b) a carbohydrate oxidizing agent and a bi-functional carbohydrate-protein linking agent, and the proteins cross-linking comprises contacting the tissue with a cross-linking reagent, wherein the cross-linking reagent is a member selected from the group consisting of glutaraldehyde, formaldehyde, a dialdehyde, carbodiimide, and a polyepoxy ether.

U.S. Patent No. 4,931,546 discloses a process for treating collagen with periodic acid or periodate and then with glutaraldehyde. U.S. Patent No. 4,931,546 does not expressly or inherently describe stabilizing glycosaminoglycans on the tissue. The Examiner correctly points out that Applicants have defined tissue as being able to be constructed from extracellular matrix

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and collagen is characterized as a component of extracellular matrix. However, even though collagen and glycosaminoglycans are components of extracellular matrix, they are very different from each other, wherein collagen is a protein and glycosaminoglycans are polysaccharides. Collagen and glycosaminoglycans have different functions in the tissue and cannot be used interchangeably. Consequently, by teaching a step of treating collagen, U.S. Patent No. 4,931,546 does not teach or suggest a step of stabilizing glycosaminoglycans on the tissue. Therefore, U.S. Patent No. 4,931,546 does not anticipate claim 1 of the invention.

Claims 2, 3, 10, 11, 34-37, 41, 42, 48 and 49 depend from claim 1 and are not anticipated by U.S. Patent No. 4,931,546 for at least the same reasons claim 1 is not anticipated.

Further, claim 1 would not be obvious in view of U.S. Patent No. 4,931,546 because it teaches away from the present invention. Teaching away from a claimed invention is essentially a *per se* demonstration of lack of *prima facie* obviousness. *In re Dow Chemical Co.*, 837 F.2d 469, 5 USPQ2d 1529 (Fed. Cir. 1988); *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Nielson*, 816 F.2d 1567, 2 USPQ2d 1525 (Fed. Cir. 1987).

U.S. Patent No. 4,931,546 teaches mixing glycosaminoglycans with collagen after collagen has been oxidized (see col. 7, lines 30-66, Examples 15-17), wherein mixing is followed by forming into a mold. Contrarily to that, the present invention teaches stabilizing glycosaminoglycans on the tissue (as defined on page 10 of the specification) as generating at least one covalent bond between a glycosaminoglycan and a molecule of the tissue other than the same glycosaminoglycan. As described in the disclosure on page 8, lines 10-25, for stabilizing on the tissue, glycosaminoglycan has to be first oxidized and then linked by a bi-functional

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carbohydrate-protein linking agent to the tissue. Thus, the reference does not teach covalently linking glycosaminoglycan to collagen.

Following U.S. Patent No. 4,931,546, one of ordinary skill in the art would have lacked motivation to use this reference to practice the method of the present invention with a reasonable expectation of success. Absent such reasonable motivation, there can be no prima facie case of obviousness. See, e.g., MPEP §2143.

Accordingly, reconsideration and withdrawal of the Section 102 (b) rejection of claims 1-3, 10, 11, 34-37, 41, 42, 48 and 49 are respectfully requested.

The Bernacca et al. reference and U.S. Patent No. 5,660,692

Claims 1-6, 10-11, 34, 41 and 42 stand rejected under 35 U.S.C. 102(b) as being anticipated by Bernacca et al. Claims 1-3, 10, 11, 34, 41 and 42 stand rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,660,692.

Claim 1 is amended to remove "heterofunctional azide reagent" and thus obviate the rejections. Claims 2-6, 10-11, 34, 41 and 42 depend from claim 1 and are not anticipated at least for the same reasons claim 1 is not anticipated.

Accordingly, reconsideration and withdrawal of the Section 102 (b) rejection of claims 1-6, 10-11, 34, 41 and 42 are respectfully requested.

U.S. Patent No. 6,166,184

Claims 1-6, 10, 11, and 12 stand rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 6,166,184. This rejection is respectfully traversed. Claim 1 as amended obviates the rejection.

The Examiner stated that "the claims are directed to a one step treatment of a tissue with

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a water soluble carbodiimide at pH 6.9-7.9." Claim 1 is directed to (1) stabilizing glycosaminoglycans (GAGs) on the tissue and (2) cross-linking proteins on the tissue. As stated in the disclosure on page 8, lines 26-29, proteins may be cross-linked before GASs are stabilized, simultaneously with GAS stabilization and preferably protein cross-linking is performed after GAG stabilization.

U.S. Patent No. 6,166,184 does not does not expressly or inherently teach stabilizing glycosaminoglycans on the tissue. Moreover, the '184 patent teaches away from the present invention, wherein it teaches first blocking amino groups of collagen and then activating carboxyl groups of collagen with carbodiimide followed by crosslinking the activated carboxyl groups using a polyfunctional spacer (see col. 7, lines 51-67, col. 8 and col. 9, lines 1-10). In the present invention, amino groups of collagen are needed for reacting with carbodiimide treated glycosaminoglycans.

The present invention was not intended to be one in which blocking amino groups on the tissue were made for purposes of cross-linking GAGs. From the disclosure (see page 6, lines 3-6), a person skilled in the art would understand that amino groups should not be blocked for the invention to work.

Further, claim 1 would not be obvious in view of the '184 patent. As stated in MPEP 2143.01, if the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification (citing *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (CCPA 1984)).

The present invention teaches utilizing amino groups while the '184 patent specifically requires blocking amino groups to avoid reacting amino groups with activated carboxyl group

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activated (see col 7, lines 34-38); thus, if the amino groups were not blocked, this would render the '184 patent being modified unsatisfactory for its intended purpose, which is cross-linking of selected groups only such as activated carboxyl groups of collagen.

Following U.S. Patent No. 6,166,184, one of ordinary skill in the art would have lacked motivation to use this reference to practice the method of the present invention with a reasonable expectation of success. Absent such reasonable motivation, there can be no *prima facie* case of obviousness. See, e.g., MPEP §2143.

Accordingly, reconsideration and withdrawal of the Section 102 (b) rejection of claims 1-6, 10, 11, and 12 are respectfully requested.

Claim Rejections – 35 USC § 103

Claims 1-6, 10, 11, and 34 stand rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 6,014,741. This rejection is respectfully traversed.

The rejection over the '741 patent is obviated by the present amendment of claim 1, from which claims 2-6, 10, 11, and 34 depend.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion of motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or reference when combined) must teach or suggest all the claim limitations. MPEP § 2143. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

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The '741 patent teaches (1) treating biomolecules comprising amine moieties and 2-aminoalcohol moieties with periodate to form aldehyde moieties, (2) reacting the aldehyde moieties of biomolecules with amine moieties of the biomaterial to form an imine moiety, and (3) stabilizing the imine moiety via reductive alkylation to form a secondary amine (see col. 5, lines 1-23). GAGs ordinary do not have amine moieties and 2-aminoalcohol moieties and would have to be specifically modified to provide such moieties.

Further, the '741 patent does not teach the use of substances other than periodate and reducing agents for cross-linking proteins on the tissue (col. 7, lines 25-56). Moreover, the '741 patent specifically teaches covalently attaching biomolecules to a biomaterial surface in the absence of glutaraldehyde or cross-linking collagen in the absence of glutaraldehyde (see col. 7, lines 42-44).

Thus, the '741 patent does not provide a suggestion or motivation to modify its teaching to produce the claimed method comprising stabilizing of glycosaminoglycans on the tissue with (b) a carbohydrate oxidizing agent and a bi-functional carbohydrate-protein linking agent.

Further, the '741 patent does not provide a suggestion or motivation for cross-linking proteins on the tissue, wherein the proteins cross-linking comprises contacting the tissue with a cross-linking reagent selected from the group consisting of glutaraldehyde, formaldehyde, a dialdehyde, carbodiimide, and a polyepoxy ether.

Further, the '741 patent does not teach or suggest all the limitations of claim 1 such as "stabilizing glycosaminoglycans on the tissue and cross-linking proteins on the tissue, wherein the glycosaminoglycans stabilizing comprises contacting the tissue with ...(b) a carbohydrate oxidizing agent and a bi-functional carbohydrate-protein linking agent, and the proteins cross-

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linking comprises contacting the tissue with a cross-linking reagent, wherein the cross-linking reagent is a member selected from the group consisting of glutaraldehyde, formaldehyde, a dialdehyde, carbodiimide, and a polyepoxy ether."

Following the '741 patent, one of ordinary skill in the art would have lacked motivation to use its teachings to perform the claimed process with a reasonable expectation of success. Absent such reasonable motivation, there can be no prima facie case of obviousness. See, e.g., MPEP §2143.

Accordingly, reconsideration and withdrawal of the Section 103 (a) rejection of claim 1 are respectfully requested. Claims 2-6, 10, 11, 34 and 40 depend from claim 1 and are not obvious for at least the same reasons claim 1 is not obvious.

For at least the reasons set forth above, it is respectfully submitted that the above-identified application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are respectfully requested.

Should the Examiner believe that anything further is desirable in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,
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